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EXAMINER

DUTT, ADITI

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Status of Application, Amendments and/or Claims

1. Applicant's amendments filed 3 May 2010 have been entered and fully considered. On reconsideration of the last Office Action and Applicant's persuasive submission that the finality was improper based on the newly cited Tropepe reference, the finality of the Final Rejection mailed 2 March 2010 has been withdrawn.
2. Claims 1-6, 11-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 27 October 2008.
3. Claims 7-8, drawn to a method for producing rhodopsin-positive retinal nerve cells by isolating and differentiating iris pigmented epithelial cells in a serum free culture medium, are being considered for examination in the instant application.

Rejection maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to

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a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The rejection of claims 7-8, under 35 U.S.C. 103(a) as being unpatentable over Haruta et al., (Nat Neurosc 4: 1163-1164, 2001), in view of Tropepe et al. (Sc. 287: 2032-2036, 2000) and in further view of Kosaka et al. (Exp Cell Res 245: 245-251, 1998), are applied to the amended claims for reasons of record in the Office Action dated 2 March 2010.
5. Applicant traverses the rejection primarily because none of the cited references of Haruta, Tropepe and Kosaka teach the differentiation of iris pigmented epithelial cells into the rhodopsin positive retinal nerve cells "without a gene transfer", rather Haruta et al teach that the transfer of Crx genes is essential to induce differentiation of iris-derived cells to become rhodopsin-positive. Applicant concedes that Haruta briefly considers the possibility of the development of iris-derived cells to photoreceptors without a gene transfer, however, Applicant alleges that it is merely "an unfounded guess" on this possibility for which no experimental results are presented. The skilled artisan would, therefore, consider that Haruta fails to teach differentiation to rhodopsin-positive cells without a gene transfer. Applicant further alleges that Tropepe neither teaches that spherical colonies can be obtained from culturing the ciliary derived cells, nor discloses the differentiation of iris pigmented epithelial cells to rhodopsin positive cells without a gene transfer. Applicant further alleges that the Tropepe reference teaches away from the claimed invention because of the express teaching that the colonies do "not arise from cells of the adult iris, ciliary

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muscleor from non-pigmented ciliary process cells ...". Applicant concludes that because of the above stated reasons, the skilled artisan would not have the motivation to modify the method with a reasonable expectation of success, therefore requests the withdrawal of the rejection. Applicant also cautions Examiner with regards to the use of impermissible hindsight.

6. Applicant's arguments have been fully considered, however, are not found to be persuasive. As stated in the previous office Action and acknowledged by Applicant, Haruta et al teach that ciliary margin cells can differentiate to rod photoreceptors (that would inherently be rhodopsin positive) **subsequent to formation of spherical colonies** along with an explicit suggestion that such cells can be cultured to obtain spheres or spherical colonies to induce differentiation to rod photoreceptors **without gene transfer** (emphasis added). It is well known that the iris and ciliary derived cells can behave similarly under similar culture conditions. It is also known that the ciliary epithelial and IPE cells are all ectodermic cells having a common developmental origin. Applicant's allegation that Haruta's "unfounded guess" on the subject of differentiation without gene transfer is not proper, simply because the reference provides the skilled artisan an explicit suggestion to achieve differentiation without introducing a gene. The skilled artisan would thus be motivated to try differentiating without a gene transfer, because it would be cheaper and more efficient, thereby leading to an "improvement" of the technique (MPEP 2144). It is reminded that obviousness can be established by combining or modifying the teachings of the prior art to

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produce the claimed invention where there is **some teaching, suggestion, or** motivation to do so. *In re Kahn*, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006) (MPEP 2143.01). It is further noted that in considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom (*In re Preda*, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968)).

7. Applicant's allegation that Tropepe is teaching away is also not relevant. Applicant is pointing to cell types that are different from ciliary margin cells. Haruta and Tropepe teach pigmented ciliary margin cells. Haruta et al teach the differentiation of ciliary margin cells to photoreceptor cells, and Tropepe teaches the proliferation of mouse pigmented ciliary margin cells to form spherical colonies. Please note that the instant claims are drawn to pigmented epithelial cells. Furthermore, it is a known fact that different cell types require different culture conditions. Since Tropepe clearly teaches the proliferation of pigmented cells from the ciliary margin cells obtained from adult mouse eyes using the in vitro spherical colony forming culture method, that results in cells that are multipotential (Figure 3), Tropepe is not teaching away from the claimed invention as alleged.

8. Applicants may argue that the examiner's conclusion of obviousness is based on improper hindsight reasoning. However, "[a]ny judgement on obviousness is in a sense necessarily a reconstruction based on hindsight

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reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper." *In re McLaughlin* 443 F.2d 1392, 1395, 170 USPQ 209, 212 (CCPA 1971).

9. Based on the above discussion, the claimed invention would be prima facie obvious to the skilled artisan over the combined teachings of the prior art. The combination of the above references proves that the knowledge and expertise for the claimed method was known in the art and the results were expected to be successful. The prima facie obviousness of the claimed invention in view of the combined references, therefore, provides sufficient reasoning, and nullifies Applicant's allegations of the improper teachings in the individual references. Applicant is reminded that "one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). "The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference.... Rather, the test is what the combined teachings of those references would have suggested to those of ordinary skill in the art." *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). See also *In re Sneed*, 710 F.2d 1544, 1550, 218 USPQ 385, 389 (Fed. Cir. 1983).

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Conclusion

10. No claims are allowed.
11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
12. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is 571-272-9037. The examiner can normally be reached on M-F.
14. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Stucker, can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
15. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
30 May 2010

/Daniel E. Kolker/
Examiner, Art Unit 1649
June 4, 2010